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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/585,727	03/17/2007	Thomas Guthner	7601/88230	7880

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LAW OFFICE OF MICHAEL A. SANZO, LLC  
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ROCKVILLE, MD 20855

EXAMINER
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BALASUBRAMANIAN, VENKATARAMAN

ART UNIT	PAPER NUMBER
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1624

MAIL DATE	DELIVERY MODE
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04/17/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/585,727	<b>Applicant(s)</b> GUTHNER ET AL.	
	<b>Examiner</b> /Venkataraman Balasubramanian/	<b>Art Unit</b> 1624	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 02 January 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 21-39 and 41 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 21-39 and 41 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

Applicants' response, which included cancellation of claim 40 and amendment to claim 21, filed on 1/2/2008, is made of record. Claims 21-39 and 41 are now pending. In view of applicants' amendment to claim 21, the 102 rejection over Stucky et al., has been obviated. However, 103 rejection made in the previous office action is maintained.

#### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

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consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 21-39 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stucky Us 5,663,340 in view of Daluge US 6,552,193.

Stucky et al., teaches the same process of making 2-amino-4, 6-dichloro-5-formamidopyrimidine without using any solvent and in one-pot as required by instant claims. See column 1-4 for details. See examples 1-6 (column 4-8). Especially see example 1, step 1.1 wherein after the formation of 2,5-diamino-4,6-dihydroxypyrimidine, solvent is removed then dimethylformamide and POCl<sub>3</sub> is added to make the intermediate which further hydrolyzed in step 1.2.

As noted above, Stucky teaches a one-pot process without using additional solvent in the step leading the formamido group at 5-position. Stucky provides adequate details of the over all process in terms of varying the proportion of reagents, temperature etc.

Instant claims require use of Vilsmeier reagent as well for the instant process. use of Vilsmeier reagent is known in the art and Daluge shows use of this reagent for formylation of 2,5-diamino-4, 6-dichloropyrimidine. See column 10, example 1.

Thus, one trained in the art would be motivated to use Vilsmeier reagent as well for the above said process. Thus, one having ordinary skill in the art at the time of the invention was made would have been motivated to employ the process taught by Stucky and Daluge to the analogous starting materials and reactants of the instant invention and expect to obtain the desired product because he would have expected the

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analogous starting materials and reactants react similarly in view of the combine teaching of the prior art. It has been held that application of an old process to an analogous material to obtain a result consistent with the teachings of the art would have been obvious to one having ordinary skill. Note *In re Kerkhoven* 205 USPQ 1069. See *In re KSR International vs. Teleflex Inc.*, 82 USPQ2d 13-85, 1397 (2007).

See also MPEP 2144.05, which says, under Optimization Within Prior Art Conditions or Through Routine Experimentation:

Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. “[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.” *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%). See also *In re Hoeschele*, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see *Merck & Co. Inc. v. Biocraft Laboratories Inc.*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied,

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493 U.S. 975 (1989); In re Kulling, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997).

This rejection is same as made in the previous office action but now excludes cancelled claim 40.

Thrust of applicants' traversal relates step b and step c of the instant process. Applicants have argued that "Applicants first react a 4,6-dichloropyrimidine derivative with water; then adjust the pH to between 1.0 and 6.0 with an inorganic base; and finally hydrolyze the product in the absence of an added solvent. Thus, Applicants have two aqueous incubation steps separated by an adjustment of pH with an inorganic base. The importance of the two incubations, pH adjustment and the absence of a solvent are discussed on page 7 of the application, lines 1-23. These read as follows:

The pH [adjustment with inorganic base] is crucial, since it controls the selective reaction of B via C to D [see reaction steps on page 1 of the application]. In the case of incorrectly selected pH, a reduced yield and/or undesired by-products in the product are obtained. According to the invention, the pH is adjusted at a defined value in the range between pH 1.0 and 6.0, preferably from pH 2.0 to 5.0, more preferably from 3.0 to 4.0, the pH being measured by means of a glass electrode at a temperature of 20°C. If appropriate, the pH can be readjusted continuously in the course of the reaction which follows by adding further base under pH control.

The further reaction is carried out by heating the aqueous mixture to a temperature of from 70 to 120°C, preferably from 80 to 100°C. In the course of a reaction time of from 1 to 20 hours, the unisolated intermediates form the desired target

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product 2-amino-4,6-dichloro-5-formamidopyrimidine. This is insoluble in the reaction mixture and can be removed, washed and dried by means of process steps familiar to those skilled in the art.

It is considered to be essential to the invention that this last reaction step is effected in the absence - even of traces - of a solvent. This is because it has been found to be capable of starting to dissolve the water-insoluble 2-amino-4,6- dichloro-5-formamidopyrimidine in the reaction mixture, which makes the pyrimidine more vulnerable to a further hydrolysis, so that the ultimate result is reduced yields and/or contamination of the product with 2,5-diamino- 4,6-dichloropyrimidine, the subsequent product of the hydrolysis”.

Applicants have asserted that the above steps are distinct from the acid hydrolysis taught in Stucky et al.

However, careful consideration of Stucky et al., will reveal that Stucky et al. also teaches the pH requirement of the process implicitly. Use of acid such acetic acid of concentrations taught therein would definitely resultant in acidic pH which will meet the instant pH requirement of 1 to 6. See column 3, lines 45-63. In addition, Stucky et al., also teaches the temperature requirement. See example 1.2.

As for the criticality of the pH, the secondary reference Daluge et al., clearly teaches use of phosphate buffer and pH maintenance during the reaction. See example 3. Thus, one trained in the art would be motivated to maintain an acidic pH as taught by both Stucky et al., and Daluge et al.

As for solvent free reaction, Daluge clearly teaches such a process as seen two reactions taught in example 3. Note Daluge teaches reaction in aqueous condition without any added solvent.

Note In re KSR International vs. Teleflex Inc., 82 USPQ2d 13-85, 1397 (2007), the court stated that

[w]hen there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense.

Such is the case with instant claims. Both the prior art cited above taken together teach the overall process for making 2-amino-4,6-dichloro-5-foramidopyrimidine including use of no solvent in the first step, appropriate temperature and pH in the aqueous hydrolysis step. While stated prior art use aqueous acid or phosphate buffer with pH adjustment, instant process adds water and neutralizes the phosphoric acid of the first step with base to arrive at the pH range. Both the prior art and instant process use aqueous condition for hydrolysis (as in Daluge). Hence, based on the teaching which provide guidance to choose various process limitations stated above, one trained in the art would be motivated to make compounds using the process including optimizing some of these limitations. Such an optimization is within the skill set of one trained in the art. Hence, such optimization would be not innovation but of ordinary skill and common sense as noted by the court.



Hence, this rejection is proper and is maintained.

***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571) 272-0662. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is James O. Wilson, whose telephone number is 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published

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applications may be obtained from either Private PAIR or Public PAG. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-2 17-9197 (toll-free).

/Venkataraman Balasubramanian/

Primary Examiner, Art Unit 1624